CERTIFICATE OF ELECTRONIC TRANSMISSION 37 C.F.R. § 1.8	
I hereby certify that this correspondence is being electronically filed with the United States Patent and Trademark Office via EFS-Web on the date below:	
January 13, 2009 Date	David L. Parker

Docket No.: CLFR:029USD1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Rosenblum *et al.*

Application No.: 10/676,725

Filed: October 1, 2003 Art Unit: 1642

For: NOVEL ANTIBODY DELIVERY SYSTEM FOR BIOLOGICAL RESPONSE MODIFIERS Examiner: Goddard, Laura B.

REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Appellants hereby submit this Reply Brief to the Board of Patent Appeals and Interferences in response to the Examiner's Answer dated November 24, 2008, making January 24, 2009 the due date.

Enclosed herewith is a Request for Oral Argument, along with the appropriate fee. Should such request or fee be deficient or absent, consider this paragraph such a request and authorization to withdraw the appropriate fee under 37 C.F.R. §§ 1.16 to 1.21 from Fulbright & Jaworski L.L.P. Account No.: 50-1212/CLFR:029USD1.

Appellants herewith file their reply to the Examiner's Answer dated November 24, 2008.

Step (b) of main claim 26 contains a key limitation that is not disclosed in or suggested by any of the art relied upon by the Examiner:

> (b) obtaining a composition comprising a protein with an antigen recognition site directed toward a cell surface associated antigen conjugated or fused to the biological response modifier, ***wherein it has been determined that cells of the patient's cancer express an antigen recognized and bound by the protein with an antigen recognition site***; and (emphasis added)

This step makes it clear that the protein composition must be selected on the basis of ***prior knowledge*** that the patient's cancer actually expressed the particular antigen being targeted ("wherein it has been determined ..."). Thus, administering the composition to a cancer patient and then ***later*** assessing whether the patient's cancer expresses the targeted antigen does not fall within the language of this claim, and indeed misses the point of the invention – the key to this invention is actually selecting the cancer patient to be treated on the basis of the antigenic profile of the cancer – and doing this ***prior*** to therapy. A similar, more recent example of such a "targeted" therapy approach is the identification of breast cancer patients whose cancer expresses her2/neu prior to administering Herceptin. However, we submit that none of the art relied on here in any way suggests testing the cancer patient prior to therapy to assess whether the tumor expresses the targeted antigen (*i.e.*, whether it would more likely be susceptible to therapy).

A review of this very lengthy Answer makes it clear that the Examiner has not met her burden of identifying such a teaching in the prior art:

(A) Claims 7, 10, 13, 14, 21, 24-29, 31 – Scannon in view of Ferris as evidenced by Kirkwood.[1]

Nowhere does the Answer explain how Scannon teaches the concept of ***pre-testing*** the patient prior to administering the immunotoxin. All that the Examiner can come forward with is that "Scannon teaches that melanoma tumor cells of melanoma patients express the 240kD antigen recognized and bound by the antibody-ricin A conjugate, therefore it was determined that the cells of the melanoma patient's cancer express the 240kD antigen ..." Answer, paragraph bridging pages 19 and 20. It is unclear what teaching the Examiner is relying on, and what the Examiner's point is – while it is true that Scannon tests melanoma cells for expression of a 240kD antigen, it in no way teaches to do so as a selection step ***prior*** to administering the immunotoxin. Earlier in the Answer, the Examiner states simply that "[t]he human patient treated with the antibody conjugate specific for melanoma would necessarily have been identified or diagnosed as a patient having a melanoma tumor and the patient's melanoma would be expressing the melanoma-specific antigen target by the antibody conjugate..." Answer, paragraph bridging pages 4 an 5. However, no where does Scannon teach to pre-test the patient prior to selecting the appropriate therapy, and the Examiner has failed to point us to language in Scannon that supports such a conclusion.

Indeed, Table 1 of Scannon teaches testing of melanoma "cell lines" from various commercial and non-commercial sources, and this Table demonstrates that not all melanomas express the targeted antigen. As stated in the text, these studies were carried out on various cell lines merely to characterize the binding specificity of the antibody ("... were conducted for the

[1] Oddly, the Examiner has re-arranged the order of rejections from the final Office Action and from our opening Brief. We are addressing the rejections in the order presented by the Examiner in her Answer.

purpose of ascertaining the binding specificity of the XMMME-001 antibody toward a number of different human melanoma cell lines ..."; col. 6, lines 11-13). This statement makes it clear that these studies are not for pre-testing cancer patients to see if they might be susceptible to therapy.

Scannon in fact teaches away from the invention! Rather than teaching to pre-screen the cancer patient, Scannon proposes an entirely distinct approach – to use a "cocktail" of various immunotoxins, in order to make it more likely that the cancer will be susceptible to at least one of the components of the cocktail. See, *e.g.*, col. 8. The fact that Scannon teaches a cocktail of different immunotoxins is strong evidence that Scannon does ***not*** contemplate pre-testing the patient (if Scannon has taught or suggested pre-testing the patient, there would be no need to teach the use of a cocktail of different immunotoxins). Indeed, the present invention circumvents the need (although does not exclude the possibility) of administering a cocktail, in that by pre-testing each patient to be treated one can determine precisely what immunotoxin should be employed in the particular patient.

B. Claim 16 Over Scannon and Ferris in view of Blick

Again, it appears as though the only reference relied upon as teaching step (b) is Scannon, which is addressed in the preceding section.

C. Claim 23 over Scannon and Ferris in view of Ghose

Again, it appears as though the only reference relied upon as teaching step (b) is Scannon, which is addressed in section A above.

D. Claims 7, 24, 26-29 and 30 over Frankel in view of Ferris

Here, the Answer is apparently relying on Frankel as teaching step (b), stating merely that "[t]he patient treated with the antibody conjugate specific for breast cancer would necessarily

have been identified of diagnosed as a patient having a breast tumor and the patient's breast cancer would be expressing the breast-cancer-specific antigen targeted by the antibody conjugate..." Answer, page 10 at bottom.

When confronted with the argument set forth above, the Examiner simply states that "Frankel did determine that the breast tumor cells of a breast tumor patient express an antigen recognized by an antibody (Table 2)" Answer, page 28 at bottom. However, this is not enough and does not meet the limitations of the claims. Table 2 is merely a screening study that was carried out "to determine how wide a range of breast cancers might be recognized by each antibody." Col. 9, lines 19-21. Nowhere that we can find does the text of Frankel in any way teach or suggest pre-testing a patient's cancer in order to determine which immunotoxin to then select and administer to the patient. Such an interpretation is borne out by the fact that in the example labeled "In Vivo Testing of Conjugates" (starting at col. 14, line 50), the test mice were simply treated with a number of different immunotoxins to see which one worked better. Such an approach is counter to the present invention, which is directed to first testing the subject to determine presence of a particular antigen, and then administering a particular composition having the correct recognition on the basis of the pre-test.

E. Claims 7, 24, 26-29, 31 over Mattes in view of Ferris

With respect to this rejection, the Answer relies on Mattes as teaching that "[t]he patient treated with the antibody conjugate specific for cervical carcinoma would necessarily have been identified or diagnosed as a patient having a cervical carcinoma and the patient's cervical carcinoma would be expressing the cervical carcinoma-specific antigen targeted by the antibody conjugate ..." Answer, paragraph bridging pages 12 and 13. In explaining this position, the Answer states that "Mattes identified cervical carcinoma from a patient that expresses MH94

antigen … and hence identified a patient having said carcinoma and determined that the patient's cancer expressed MH94 antigen…" Answer, page 32. However, the claims require that the patient be screened prior to treatment, which is nowhere to be found in Mattes as far as Appellants can find. Indeed, we have reviewed those sections dealing with the MH94 antigen, as well as other sections, and can find no teaching that would appear to support the position the Mattes teaches to pre-test patients prior to administering a particular immunotoxin, and the Examiner has pointed us to none.

F. Conclusion

We are of the opinion that the Examiner is attempting to disregard the plain language of the claims, and is positing that merely knowing that some cancer types express a particular antigen and then administering a particular construct to a patient having the same variety of cancer, is enough to defeat the pending claims. We strongly disagree. The claim language requires testing the cancer of that particular patient and then administering to that patient a composition that is known in advance to interact with the cancer tested from that particular patient. Merely knowing that cancers of that type can potentially express a particular antigen is not what this invention concerns.

For all of the foregoing reasons, the Board is requested to reverse the Examiner's conclusion of obviousness.

Dated: January 13, 2009

Respectfully submitted,

By_____

David L. Parker
Registration No.: 32,165
FULBRIGHT & JAWORSKI L.L.P.
600 Congress Ave., Suite 2300
Austin, Texas 78701
(512) 536-3055
(512) 536-4598 (Fax)
Attorney for Applicant